

### **REMARKS**

Claims 1, 161, 169 are amended in this paper without disclaimer or prejudice. Upon entry of the claim amendments, claims 1-169 are pending in this application, of which claims 1, 2, 161-163, and 169 are pending for further examination on the merits, while claims 3-160, and 164-168 are withdrawn.

Claims 1 and 169 are amended. Support for the amendments can be found throughout Applicants' specification including the original claims, especially in claim 1 as originally presented.

Claim 161 is also amended. Support for the amendments can be found in the as-filed claim.

No new matter has been introduced.

Amendment to any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the Office Action, and was done solely to expedite prosecution of this application.

Applicants respectfully reserve the right to pursue any non-elected, cancelled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications. Reconsideration of the application is requested in view of the remarks herein.

### **Claim Rejection under 35 U.S.C. §103(a)**

Claims 1, 2, 161-163, and 169 are rejected in the Office Action under 35 U.S.C. §103(a) as allegedly obvious over Yamamoto *et al.* (Chemical & Pharmaceutical Bulletin (1997), 45(8), 1282-1286; hereinafter "Yamamoto"). The Office Action asserts that the claimed compounds represent positional isomers and/or adjacent homologs of compounds disclosed in Yamamoto, and that the claimed compounds would be *prima facie* obvious to one of ordinary skill in the art (see pages 3 and 4 of the Office Action). Applicants strongly disagree and hereby traverse.

To properly determine a *prima facie* case of obviousness, the Examiner "must step backward in time and into the shoes worn by the hypothetical 'person of ordinary skill in the art' when the invention was unknown and just before it was made." M.P.E.P. § 2142. This is important as "impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art." *Id.* Three criteria may be helpful in

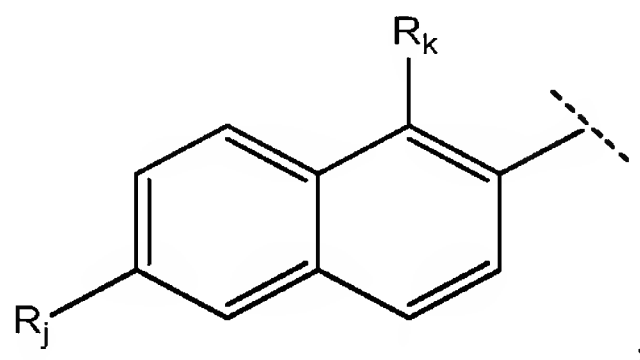
determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). "Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious." *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir. 2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

With respect to cases involving new chemical compounds, a *prima facie* case of obviousness requires "that the 'prior art would have suggested making the specific molecular modification necessary to achieve the claimed invention'". *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350 (Fed. Cir. 2007). The *Takeda* court acknowledged "the importance of identifying 'a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does' in an obviousness determination". *Id.* The issue is whether or not there is a reason "that would have led a chemist to modify a known compound in a *particular manner* to establish *prima facie* obviousness of a new claimed compound". *Id.*

Applicants further note that Yamamoto does not provide any express motivation or suggestion to one of ordinary skill in the art to make any modification on its compounds, let alone the specific modifications required to achieve the claimed compounds. Since Yamamoto does not offer any clear and specific guidance (indeed, no guidance at all), Applicants submit that Yamamoto fails to teach or suggest Applicants' claimed subject matter. As such, Applicants submit that the Office fails to establish a *prima facie* case of obviousness of the claimed subject matter over Yamamoto (especially under the *Takeda* standards).

Nevertheless, for the sole purpose to facilitate the prosecution of this application and without conceding in any way to the rejections set forth in the Office Action,

Applicants respectfully point out that the pending claims do not recite naphthoylguanidine compounds with halo and/or alkyloxy substituents attached to the naphthyl moiety; in other words, when  $R_1$  in Formula I is

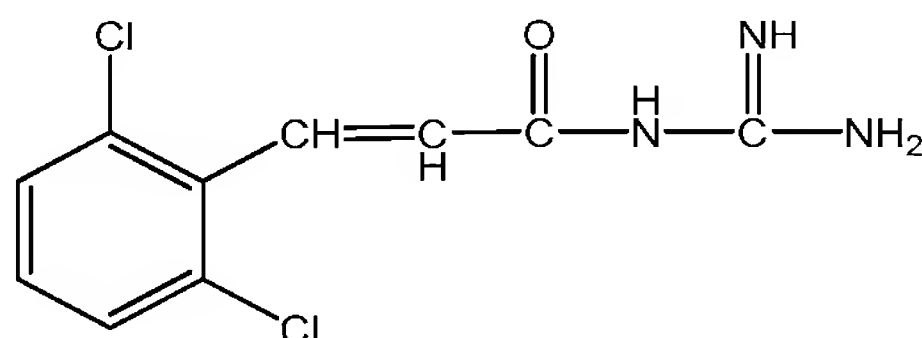


$R_k$  cannot be H, halo or  $C_{1-5}$ alkyloxy, and  $R_j$  cannot be either halo or  $C_{2-5}$ alkyloxy (see pending claim 1). In contrast, the Yamamoto compounds are all naphthoylguanidine compounds with a naphthyl moiety unsubstituted or substituted by bromine or methoxy group(s). Accordingly, Applicants submit that the compounds recited and claimed herein are distinct in structure over the compounds disclosed in Yamamoto, and are not taught or suggested by Yamamoto.

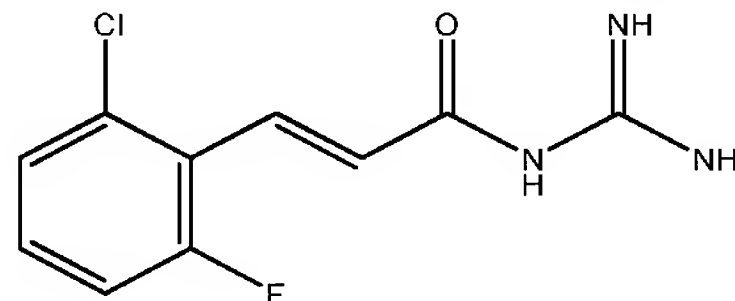
In view of the foregoing discussions, Applicants submit that claims 1, 2, 161-163, and 169 are patentable over Yamamoto. Therefore, reconsideration and withdrawal of the rejection of these claims under 35 USC § 103(a) over Yamamoto is respectfully requested.

Claims 1, 2, 161-163, and 169 are rejected in the Office Action under 35 U.S.C. §103(a) as allegedly obvious over Bream (Arzneimittel-Forschung (1975), 25(10), 1477-82; hereinafter "Bream"). The Office asserts that the claimed compounds are *prima facie* obvious to one of ordinary skill in the art through replacing a halogen atom (that is, chlorine) in a Bream compound with a fluorine atom (see page 7 of the Office Action). Applicants strongly disagree and hereby traverse.

First, the Office asserts that "[A]pplicants claim fluoro replacement for chloro, at the same position" of the Bream compound (see page 7 of the Office Action). In particular, the Office refers to a compound disclosed in Bream with the following structure:

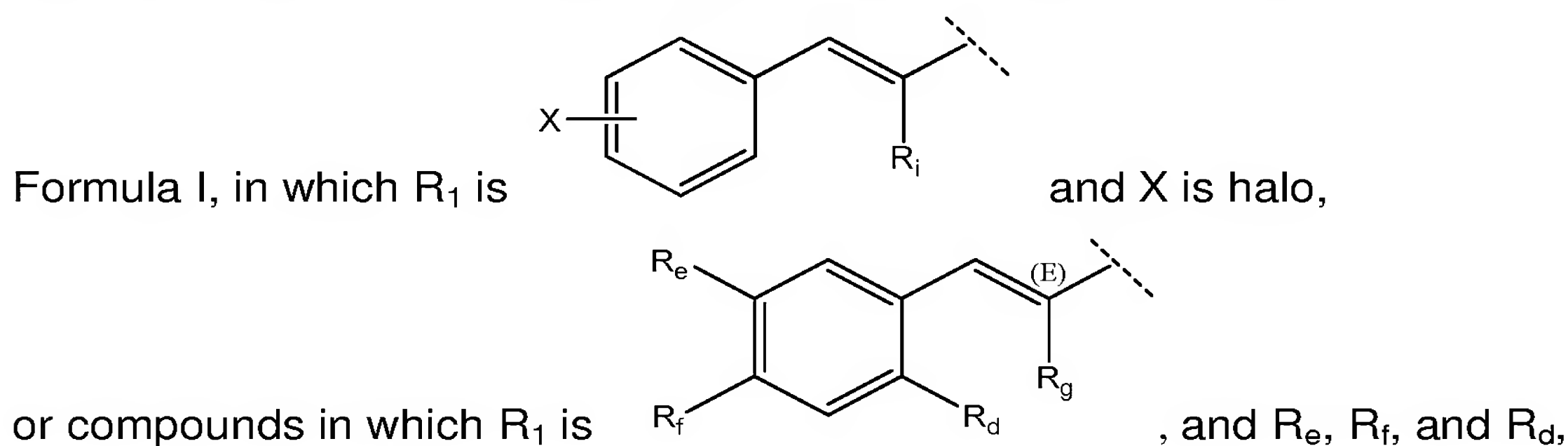


(see page 6 of the Office Action mailed August 12, 2009, and page 7 of this Office Action). In contrast to the Office's understanding, Applicants again submit that the claims of this application do not encompass any cinnamoylguanidine compounds with a



2,6-di-halo-substituted phenyl moiety (such as, as asserted in the August 2009 Office Action). Indeed, the difference between the presently claimed compounds and those described in the Bream reference is more than just a simple replacement of one halogen with another as asserted in the Office Actions.

However, for the sole purpose to facilitate the prosecution of this application and without conceding in any way to the rejection(s) set forth in the Office Actions, Applicants submit that the pending claims of this application do not recite compounds of



independently, are halogen. Accordingly, Applicants submit that the presently claimed compounds are not taught or suggested by Bream.

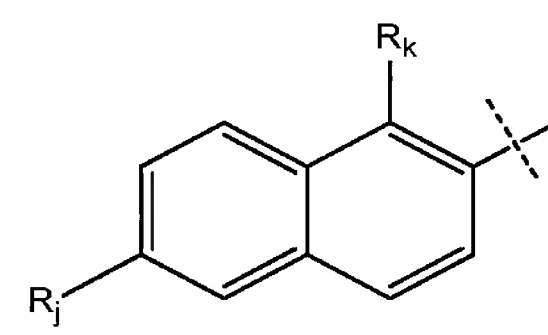
As such, Applicants submit that claims 1, 2, 161-163, and 169 are patentable over Bream. Therefore, reconsideration and withdrawal of the rejection under 35 USC § 103(a) over Bream is respectfully requested.

Claims 1, 2, 161-163, and 169 are rejected in the Office Action under 35 U.S.C. §103(a) as allegedly obvious over Yamamoto in view of Bream. The Office asserts that the claimed compounds are *prima facie* obvious to one of ordinary skill in the art through combining the known elements taught in Yamamoto and Bream (see page 7 of the Office Action). Applicants respectfully disagree and hereby traverse.

Applicants submit that the above reasoning in rebutting the obviousness rejections over Yamamoto or Bream is applicable in this section of the discussion, that is, the compounds recited and claimed in the pending claims are distinct in structure

from those disclosed in Yamamoto or Bream, and have not been taught or suggested by Yamamoto or Bream, either alone or in combination. Indeed, Yamamoto and Bream, either alone or in combination, fail to teach or suggest all of the elements of Applicants' claimed subject matter.

Applicants herein submit that the combination of Yamamoto and Bream fails in rendering the claimed compounds obvious. In brief, the pending claims of this application **do not** encompass compounds with R<sub>1</sub> in Formula I being a naphthyl moiety



that is unsubstituted or substituted by halo or alkyloxy (that is, R<sub>1</sub> is R<sub>j</sub>, R<sub>k</sub> is hydrogen, halo or C<sub>1-5</sub>alkyloxy, and R<sub>j</sub> is halo or C<sub>1-5</sub>alkyloxy). The pending claims **do not** encompass cinnamoyl compounds (of Formula I) having the phenyl moiety at the R<sub>1</sub> position being substituted by halogen or C<sub>1-5</sub>alkyloxy group(s) (see claim 1). In contrast, Applicants note that the compounds disclosed in Yamamoto and Bream have the corresponding R<sub>1</sub> group being a phenyl or naphthyl group, wherein the phenyl/naphthyl group is either unsubstituted or substituted by halo (Bromine or Chloro) or methoxy substituents (applying the definitions in Formula I; see page 7 of the August 2009 Office Action).

Applicants submit again that neither Yamamoto nor Bream provides any express motivation or suggestion to one of ordinary skill in the art to make modifications on their compounds to reach the claimed compounds. Indeed, in view of the structural differences between the Yamamoto compounds (i.e., naphthyl compounds) and the Bream compound(s) (i.e., phenyl compounds), Applicants submit that one skilled in the art would not even make attempts in combining their teachings, let alone be motivated to make specific modifications based on various elements allegedly taught therein to reach the claimed compounds. Accordingly, Applicants submit that claims 1, 2, 161-163, and 169 are patentable over Yamamoto in view of Bream.

In view of the foregoing discussions, Applicants submit that the claimed subject matter of this application is patentable over Yamamoto and Bream, either alone or in combination. Therefore, reconsideration and withdrawal of all the rejections under 35 USC § 103(a) is proper and the same is requested.

### **CONCLUSIONS**

In view of the above amendments and remarks, each of the pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call one of Applicant's undersigned representatives to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge any credits or deficiency in the fees filed (or with any paper hereafter filed in the fees filed (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 64681(70403).

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Customer No: 21874

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